Release of active ingredients from cosmetic emulsions

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Introduction

Fast development of cosmetic industry and increasing awareness about healthy appearance have prompted the need for improved quality of cosmetic products and stimulated development of new methods aimed at characterisation and performance of new products. One of the fundamental tests of cosmetic preparations is that for bioavailability, which permits determination of identical composition and performance of the series of products made at certain time intervals. Tests of bioavailability involve determination of the kinetics of release of the active ingredient from the semi-solid cosmetic formulation such as emulsion, gel, etc.

Description of the procedure of the release of active substances cosmetic emulsions

Emulsion is a thermodynamically unstable system made of two immiscible liquids, and one of the liquids is dispersed in the other in the form of small droplets. Cosmetic formulations in the form of emulsions are most often used for cosmetic products for skin care. This formulation is conducive to appropriate lipid supplementation, moisturizing and nourishment of the skin. The main task of such formulations is to maintain the moisture-lipid equilibrium in the epidermis, smoothing of the skin and improvement in its elasticity. Emulsions can be divided into different types. The O/W type emulsions are those in which the oil phase is dispersed in water. This type systems show unlimited miscibility with water and quick penetration through the skin with simultaneous production of a thin protective film on the skin surface. This type emulsions are the formulations for day use UV protecting, nourishing, regenerating and moisturizing cosmetics [1, 2].

In the W/O emulsions the water phase is dispersed in the oil phase. Such systems show unlimited miscibility with oil, on an attempt to add water a characteristic roll-like structures appear. Upon application on the skin the W/O emulsions leave a more oily film on the skin surface than O/W ones, and this film prevents the through epithelium water loss (TEWL). Usually this type of formulation is used for regenerative-nourishing night creams, semi-oily day creams: care-protectiveand moisturizing ones [1, 2]. Multiple emulsions of O/W/O and W/O/W type are the multiphase systems and each of the component phases contains the dispersed droplets of the other phase. This type formulations are used when the active ingredients added to the preparations are highly sensitive, hardly miscible or are to be released with delay [1, 3 – 5].

The active substances can penetrate the stratum corneum (the outer layer of epithelium) via two ways: the transepidermal one, through corneocytes (intracellular) or through intercellular cement (intercellular) and the transfollicular one, through adnexa cutis, i.e. sweat glands, sebaceous glands and hair follicles. Only small particles can penetrate through the hydrophilic corneoytes.

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The transport of amphiphilic and lipophilic substances through the stratum corneum is realised through the lipid intracellular cement. The only way of penetration of ions and large molecules through the stratum corneum involves the anexa cutis. The transfollicular penetration permits the active substance to reach the deepest layer as hair follicules are set in the dermis. The choice of transepidermal way depends on the physiological and physicochemical properties of the active substance [6, 7]. The physiological factors concern the skin physiognomy, its state and age, the skin area treated, the thickness of stratum corneum, and the degree of the skin moisture content. The physicochemical factors are closely related to the active and the ancillary ingredients. The skin devoid of stratum corneum loses water diffusing to its surface and this loss of moisture content is not prevented even by application of a cellophane film applied [6, 7]. Without stratum corneum, the skin becomes permeable for many therapeutic substances, for instance, the skin without stratum corneum permeates 78-90% of the active ingredient, while the skin with stratum corneum permeates only 1-2% of this ingredient [6]. In persons who suffer from diseases attacking stratum corneum, the enhanced permeation through skin is observed. Easier penetration of active substances is related to the reduction or elimination of the hydrophilic coat that can achieved by the use of surfactants or solvents. The influence of a solvent on permeabilityof salicylates chosen as a group of active ingredients, through the skin has been studied in [7]. Another method for increasing the rate of penetration involves the elevation of the moisture content of the skin ensured by the occlusive dressing. Very important for the transepidermal penetration rate of active substances is the thickness of stratumcorneum. The parts of human body can be ordered according to increasing permeability as follows: skin of forearm, sole of foot, skin of the head with hair, abdomen, upper part of the thigh, crouch and back of the ear [8, 9]. The amount of the active ingredient absorbed in a given time per a unit of area increases with increasing concentration of this active ingredient. At a constant concentration, greater amount of the active ingredient is absorbed when it is permeated through a larger area. A change in pH, affecting the process of dissociation, causes an increase in absorption of the active ingredient if it also results in an increase in the number of nonpolar particles [10].

The rate of penetration also depends on the molecules of a given compound, in particular the size and shape. The rate of absorption is inversely proportional to the molecular mass of the compound, small particles penetrate faster than large ones, although the relation between their size and rate of release holds only in a certain range [10]. The parameter that describes the properties of stratum corneum and permits concluding on a substance permeability inside this layer is the oil/water partition coefficient. The substances of lyophilic character are hardly released from the base of emulsion of the same character, although they easily penetrate the lipid structures of the intercellular cement. The greater the lyophilicity of a compound, the lower its dissolution in water and the lower the possibility of its penetration inside the deeper and more hydrophilic layers of epidermis [11].

Determination of the release of active ingredients allows quantification of the bioavailability of the active ingredients contained in cosmetic emulsions. Results of the release measurements permit assessment of the quality of a given formulation. The release measurements are performed at the first stage of working out the cosmetic formulations and in later phases of life cycle of the new product, in order to confirm the repeatability of the process of production for each series of cosmetic products [12, 13]. The ability of diffusion of the active ingredient from the cosmetic base through a membrane to a proper solvent is evaluated. To obtain reliable and reproducible results many factors should be taken into regard. The most important are the proper choice of the membrane filter that imitates the skin barrier, the type of accepting liquid and temperature of the process.

Membranes used for evaluation of release of the active ingredients form cosmetic emulsion should be characterised by specific porosity to facilitate the diffusion of the active substance. The best results are obtained when the membrane is characterised by high porosity, minimum thickness and is neutral towards the accepting liquid and emulsion base [14, 15]. Membranes are responsible for curbing the formulation studied, protect against changes in the area of release and against penetration of the ancillary substances into the accepting liquid. The measurements of the process are made for hydrophobic membrane filters based on polysulphones, cellulose acetate or a natural animal skin [12 – 14]. It is recommended that the acceptor liquid (medium) has properties similar to the physiological fluid.The active ingredient studied should be soluble in the medium. A very important parameter influencing the results is the pH of the accepting liquid. It should be established taking into regard: (a) pH of the cosmetic formulation studied, (b) pH at which the active ingredient dissolves in the accepting liquid and (c) pH of the membrane used for the release study [13, 14]. The optimum pH of the accepting liquid should be close to that of human skin (pH 5-6). When the active ingredient dissolves in water the accepting liquid most often used in phosphate buffer, while if it does not dissolve in water, the most popular accepting liquid is a water-alcohol solution. Measurements of the active ingredient release from cosmetic formulations are most often made at 25, 32 or 37°C. The duration of measurements depends on the solubility of the active ingredient studied [16]. In order to get reliable results it is recommended to perform 6 independent measurements. To make the measurement, the extraction cuvettes are filled with a certain amount of a given cosmetic formulation, as shown in Figure 1, the cuvettes are covered with the selected membrane imitating human skin, then an O-ring is fitted to protect the membrane against movements. The cuvettes with the membrane and the ring are capped to make sure that the membrane is well stretched and did not contain air bubbles.

Fig. 1. Cuvettes used for determination of release rate of active ingredients from cosmetic formulations

Table 1

Examples of substances used in cosmetics to be tested release

No.	Name of the active ingredient	Apparatus	Literature
Pharmaceutical means			
1	Sodium diclofenac (pain killer)	Dissolution apparatus FPVI- Varian 7025	20
2	Heparin (anticoagulant activity)	Dissolution apparatus VK-7010	21
3	Hydrocortisone acetate (anti-inflammatory activity)	Franz chamber	22
Antioxidants			
4	Polyphenols (anti-inflammatory activity, bactericidal activity)	Franz chamber	23
5	Rutin (blood vessel protection, inhibition of angiogenesis)	Franz chamber	24
Vitamins and related compounds			
6	(d)-alpha-tocopherol – vitamin E (antiaging, hinders skin ageing related to the effect of active oxygen species)	Franz chamber	25
7	Retinyl acetate–provitaminA (stimulating and regulating skin cell growth, antiaging effect)	Franz chamber	25
8	Ascorbic acid–vitamin C (antiaging effect)	Franz chamber	25
9	Pyridoxine –vitamin B6 (stimulates processes of skin healing)	Franz chamber	25
10	Retinoic acid (exfoliating and antiaging effect)	Franz chamber	26
11	Isotretinoin (anti-acne effect)	Diffusion chamber VK- 7010	21
12	Nicotinamide - vitamin B2 (bacteriostatic effect)	Franz chamber	27
Vegetable oils and extracts			
13	Thyme extract	Membrane technique Mutimer apparatus	28
14	Palm oil (calming and skin nourishing agent)	Franz chamber	29
Alkaloids			
15	Capsaicin (hindering prostate tumour growth)	Franz chamber	30
UV Filters			
16	OctylMethoxycyanammonate (OMC) (protecting against UV radiation)	Franz chamber	31
Carboxylic acids			
17	Salicylic acid (exfoliating and bactericidal agent)	Franz chamber	22
Sugar derivative			
18	Arbutin (skin lightening agent)	Apparatus 600 HH, Erweka	32
19.	Cyclodextrin(odour absorbent)	Franz chamber	33

A few apparatuses have been designed and proposed for the measurements of release rate of the active ingredient from cosmetic formulations. One of them is a flow-through apparatus proposed by Van Kelwith the chamber system. However, the most popular since 1978 has been the Franz chamber. It is composed of two parts: a water bath and a chamber filled with the accepting liquid. The accepting liquid is stirred by a magnetic stirrer and collected at certain intervals in certain amounts [17]. Thus, the amount of the active ingredient that has passed through the membrane to the accepting liquid in a given time interval is measured. The release rate of the active ingredient can be calculated from a number of equations, although the most popular is the Higuchi one (1) [18, 19]:

$$M_t/M_0 = Kt^{1/2} \quad (1)$$

where: M_t – the amount of the active ingredient released in time t, M_0 – the initial amount of the active ingredient, t–time

The amount of the released active ingredient in time is calculated from the equation:

$$\%\ \text{of the substance released} = \left(\frac{A_p}{A_w}\right)\left(\frac{m_w[mg] \times C_w}{V_w[ml]}\right)\left(\frac{1}{D_w}\right)\left(\frac{V_p[ml]}{m_p[ml]}\right) \times 100\% \quad (2)$$

where

A_p – absorbance of the sample [-],
A_w – absorbance of the standard [-],
m_w – mass of the standard [mg],
V_w – volume of the standard solution [ml],
C_w – standard purity,
D_w – standard dilution,
m_p – mass of the active ingredient in the sample [mg],
V_p – volume of the medium [ml].

Results of measurements are presented as a plot of the amount of the active ingredient released versus time. The plot should be linear.

The bioavailability of the active substance can verify thequality of the semi-solid forms of cosmetics. Table I gives the names of substances whose release rate has been measured and the information on the apparatus used for the purpose.

Conclusions

The bioavailability of the active substance in cosmetic formulations is a complex process influenced by a number of factors. Pharmaceutical bioavailability study can examine how the release rate of the active substance changes during the application of the formulation, e.g. what is the influence of the evaporation of someingredients contained in the cream. Such studies are a good test of the quality of products and the reproducibility of production.

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